

WHAT WE CLAIM IS:

1. A nucleic acid comprising a nucleotide sequence encoding a human *hiwi* gene.
2. A nucleic acid according to Claim 1 wherein the human *hiwi* gene has a nucleotide sequence that encodes an amino acid sequence identified by SEQ ID No. 2..
3. A homogeneous composition of a human *hiwi* gene product having a molecular weight of about 90 kilodaltons and an amino acid sequence identified by (SEQ ID No.: 2).
4. A nucleic acid hybridization probe comprising a nucleotide sequence identified by Seq ID No. 1.
5. A recombinant expression construct comprising a nucleic acid having a nucleotide sequence encoding a human *hiwi* gene according to Claim 1, wherein the construct is capable of expressing the human *hiwi* gene product in a transformed culture of eukaryotic or prokaryotic cells.
6. A recombinant expression construct according to Claim 5 wherein the human *hiwi* gene has a nucleotide sequence that encodes an amino acid sequence identified by SEQ ID No.: 2.
7. A cell culture transformed with the recombinant expression construct of Claim 5 wherein the transformed cell culture expresses the human *hiwi* gene.
8. A cell culture transformed with the recombinant expression construct of Claim 6, wherein the transformed cell culture expresses the human *hiwi* gene.
9. A method of screening a compound for modulating human *hiwi* gene activity in cells expressing the human *hiwi* gene product, the method comprising the steps of:
 - (a) transforming a host cell with a recombinant expression construct encoding a human *hiwi* gene according to Claim 1, wherein the cells of the transformed cell culture express the human *hiwi* gene product; and
 - (b) assaying the transformed cell culture with the compound to determine whether the compound modulates activity of the human *hiwi* gene product.
10. The method of Claim 9 wherein the human *hiwi* gene has a nucleotide sequence that encodes an amino acid sequence identified by SEQ ID No.: 2.
11. A method of Claim 9 comprising the additional step of:

- (c) comparing the compound's modulation of human *hiwi* gene activity with modulation mediated by additional compounds that are known to modulate human *hiwi* gene activity.

12. A nucleic acid comprising a nucleotide sequence encoding a human *hiwi* gene that hybridizes to a nucleic acid having a nucleotide sequence identified by Seq. ID No. 1, under conditions of 37°C in a buffer comprising 50% formamide, 1% sodium dodecyl sulfate, 5X SSC, 50µg/mL denatured salmon sperm DNA, and 5X P-buffer comprising 0.25M Tris, pH 7.5, 0.5% sodium pyrophosphate, 0.5% SDS, 1% bovine serum albumin, 1% polyvinylpyrrolidone and 1% Ficoll.

13. A nucleic acid according to claim 12, wherein the nucleic acid hybridizes to a nucleic acid having a nucleotide sequence identified by Seq. ID No. 1, under washing conditions of 10 minutes at room temperature in a wash solution of 2X SSC/ 1% SDS, followed by 10 min at 60°C in 2X SSC/ 1% SDS, followed by 5 min at 60°C in 0.5X SC/ 1% SDS.

14. A cell membrane preparation comprising a human *hiwi* gene product or derivative thereof having a molecular weight of about 90 kilodaltons and an amino acid sequence identified by SEQ ID No.: 2.

15. A cytosolic preparation comprising a human *hiwi* gene product or derivative thereof having a molecular weight of about 90 kilodaltons and an amino acid sequence identified by SEQ ID No.: 2.

16. A cell nuclear preparation comprising a human *hiwi* gene product or derivative thereof having a molecular weight of about 90 kilodaltons and an amino acid sequence identified by SEQ ID No.: 2.

17. A method for identifying a compound that induces or increases *hiwi* gene expression in mammalian cells, the method comprising the steps of:

- a) culturing a mammalian cell under conditions wherein the cell does not express the *hiwi* gene or expresses an amount of the *hiwi* gene product insufficient to repress cell proliferation;
- b) contacting the cell with a test compound for a time period;
- c) assaying the cells at intervals during the time period for *hiwi* gene expression and cell proliferation or apoptosis; and
- d) identifying compounds that induce *hiwi* gene expression, and concomitantly decrease cell proliferation or increase the percentage of cells undergoing apoptosis or both.

18. The method of claim 17, wherein the cells are human cells.

19. The method of claim 18, wherein the cells are leukemia cells or hematopoietic stem cells.

20. The method of claim 18, wherein the cells are human leukemia cells or
5 human hematopoietic stem cells.

21. A method for increasing retention of primitive CD34⁺ hematopoietic stem cells in an *in vitro* bone marrow or peripheral blood culture, the method comprising the step of culturing the bone marrow or peripheral blood culture in the presence of a compound identified by the method of claim 17.

10 22. A method for increasing retention of primitive CD34⁺ hematopoietic stem cells in an *in vitro* bone marrow or peripheral blood culture, the method comprising the step of introducing into the primitive CD34⁺ hematopoietic stem cells a recombinant expression construct according to claim 5.

23. A method according to claim 22, wherein the recombinant expression
15 construct comprises a retroviral or lentiviral vector.

24. A method according to claim 22, wherein expression of the hiwi gene product by the recombinant expression construct is inducible expression.